Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJDA1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

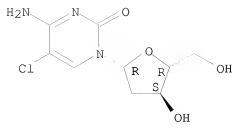
NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	NOV 21	CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from 2004-present
NEWS 3	NOV 26	MARPAT enhanced with FSORT command
NEWS 4	NOV 26	CHEMSAFE now available on STN Easy
NEWS 5	NOV 26	Two new SET commands increase convenience of STN searching
NEWS 6	DEC 01	ChemPort single article sales feature unavailable
NEWS 7	DEC 12	GBFULL now offers single source for full-text coverage of complete UK patent families
NEWS 8	DEC 17	Fifty-one pharmaceutical ingredients added to PS
NEWS 9	JAN 06	The retention policy for unread STNmail messages will change in 2009 for STN-Columbus and STN-Tokyo
NEWS 10	JAN 07	WPIDS, WPINDEX, and WPIX enhanced Japanese Patent Classification Data
NEWS 11	FEB 02	Simultaneous left and right truncation (SLART) added for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 12	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 13	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS 14	FEB 10	COMPENDEX reloaded and enhanced
NEWS 15	FEB 11	WTEXTILES reloaded and enhanced
NEWS 16	FEB 19	New patent-examiner citations in 300,000 CA/CAplus patent records provide insights into related prior art
NEWS 17	FEB 19	Increase the precision of your patent queries -- use terms from the IPC Thesaurus, Version 2009.01
NEWS 18	FEB 23	Several formats for image display and print options discontinued in USPATFULL and USPAT2
NEWS 19	FEB 23	MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS 20	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS 21	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters
NEWS 22	FEB 25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS 23	MAR 06	INPADOCDB and INPAFAMDB enhanced with new display formats
NEWS 24	MAR 11	EPFULL backfile enhanced with additional full-text applications and grants
NEWS 25	MAR 11	ESBIOBASE reloaded and enhanced
NEWS 26	MAR 20	CAS databases on STN enhanced with new super role for nanomaterial substances
NEWS 27	MAR 23	CA/CAplus enhanced with more than 250,000 patent equivalents from China

```
 NEWS 28  MAR 30  IMSPATENTS reloaded and enhanced

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN customer
  agreement.  This agreement limits use to scientific research.  Use
  for software development or design, implementation of commercial
  gateways, or use of CAS and STN data in the building of commercial
  products is prohibited and may result in loss of user privileges
  and other penalties.

* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:49:17 ON 31 MAR 2009

=> FIL REGISTRY
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22

FILE 'REGISTRY' ENTERED AT 13:49:29 ON 31 MAR 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   29 MAR 2009  HIGHEST RN 1129300-01-1
DICTIONARY FILE UPDATES:  29 MAR 2009  HIGHEST RN 1129300-01-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> E "5-CLDC"/CN 25
E1            1     5-CIS-SPIRILLOXANTHIN/CN
E2            1     5-CL-PADAB/CN
E3            0 --> 5-CLDC/CN
E4            1     5-CORRINCARBONITRILE,
1,2,3,24-TETRADEHYDRO-8,8,13,13,18,18,19-HEPTAMETHYL-, NICKEL COMPLEX/CN
E5            2     5-CORRINCARBONITRILE,
1,2,3,4-TETRADEHYDRO-4,21-DIHYDRO-8,8,13,13,18,18,19-HEPTAMETHYL-, COBALT COMPLEX/CN
E6            1     5-CORRINCARBONITRILE,
1,2-DIDEHYDRO-8,8,13,13,18,18,19-HEPTAMETHYL-, COBALT COMPLEX/CN
```

```
E7            1     5-CORRINCARBONITRILE,
1,2-DIDEHYDRO-8,8,13,13,18,18,19-HEPTAMETHYL-, NICKEL COMPLEX/CN
E8            1     5-CORRINCARBONITRILE, 1,8,8,13,13-PENTAMETHYL-/CN
E9            1     5-CORRINCARBONITRILE, 1,8,8,13,13-PENTAMETHYL-, NICKEL COMPLEX/CN
E10           1     5-CORRINCARBONITRILE, 1,8,8,13,13-PENTAMETHYL-, NICKEL COMPLEX,
(1R*,19R*)-/CN
E11           1     5-CORRINCARBONITRILE, 1,8,8,13,13-PENTAMETHYL-, NICKEL COMPLEX,
STEREOISOMER/CN
E12           2     5-CORRINCARBONITRILE, 1-FORMYL-8,8,13,13,18,18,19-HEPTAMETHYL-,
NICKEL COMPLEX, (1R*,19R*)-/CN
E13           1     5-CORRINCARBONITRILE,
2,3-DIDEHYDRO-8,8,13,13,18,18,19-HEPTAMETHYL-, NICKEL COMPLEX/CN
E14           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-/CN
E15           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-,
(1R,19R)-REL-/CN
E16           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-, COBALT
COMPLEX/CN
E17           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-,
MONOHYDROCHLORIDE/CN
E18           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-,
MONOHYDROCHLORIDE, (1R,19R)-REL-/CN
E19           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-,
MONOHYDROCHLORIDE, (1R,19R)-REL-, COMPD. WITH ETHANOL (1:1)/CN
E20           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-,
MONOHYDROCHLORIDE, TRANS-(±)-/CN
E21           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-,
MONOHYDROCHLORIDE, TRANS-(±)-, COMPD. WITH ETHANOL (1:1)/CN
E22           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-, NICKEL
COMPLEX, (1R*,19R*)-/CN
E23           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-, NICKEL
COMPLEX, TRANS-/CN
E24           2     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-, RHODIUM
COMPLEX/CN
E25           1     5-CORRINCARBONITRILE, 8,8,13,13,18,18,19-HEPTAMETHYL-, RHODIUM
COMPLEX, (1R*,19R*)-/CN

=> E "CLDC"/CN 25
E1            1     CLD 80/CN
E2            1     CLDADO/CN
E3            0 --> CLDC/CN
E4            1     CLDN1 PROTEIN (HUMAN CLONE DNA52185 GENE UNQ481)/CN
E5            1     CLDN10 PROTEIN (MOUSE STRAIN CZECH II CLONE IMAGE:3501011 GENE
CLDN10)/CN
E6            1     CLDN10 PROTEIN (MOUSE STRAIN FVB/N CLONE MGC:30291
IMAGE:5040100)/CN
E7            1     CLDN11 PROTEIN (HUMAN CLONE MGC:9232 IMAGE:3895040)/CN
E8            1     CLDN17 PROTEIN (HUMAN CLONE DNA73737 GENE UNQ758)/CN
E9            1     CLDN18 PROTEIN (HUMAN CLONE DNA73734 GENE UNQ778)/CN
E10           1     CLDN19 PROTEIN (HUMAN CLONE MGC:40523 IMAGE:5207628)/CN
E11           1     CLDN2 PROTEIN (HUMAN CLONE MGC:88250 IMAGE:30322852)/CN
E12           1     CLDN23 PROTEIN (HUMAN CLONE IMAGE:4639904 GENE CLDN23)/CN
E13           1     CLDN3 PROTEIN (MOUSE STRAIN FVB/N CLONE MGC:13769
IMAGE:4217040)/CN
E14           1     CLDN4L1 PROTEIN (XENOPUS LAEVIS CLONE MGC:81414 IMAGE:6635231
GENE CLDN4L1)/CN
E15           1     CLDN5-PROV PROTEIN (XENOPUS TROPICALIS CLONE MGC:89185
IMAGE:7016719 GENE CLDN5-PROV)/CN
E16           1     CLDN6 PROTEIN (HUMAN CLONE DNA73736 GENE UNQ757)/CN
E17           1     CLDN6-PROV PROTEIN (XENOPUS LAEVIS CLONE MGC:81720 IMAGE:6865216
GENE CLDN6-PROV)/CN
E18           1     CLDN7 PROTEIN (DANIO RERIO CLONE MGC:76832 IMAGE:6961476)/CN
E19           1     CLDN7 PROTEIN (DANIO RERIO STRAIN AB CLONE MGC:55228
IMAGE:3819607)/CN
```

```
E20             1       CLDN8 PROTEIN (HUMAN CLONE DNA73735 GENE UNQ779)/CN
E21             1       CLDN8 PROTEIN (HUMAN CLONE MGC:24067 IMAGE:4594155)/CN
E22             1       CLDNE PROTEIN (DANIO RERIO CLONE MGC:77738 IMAGE:7000808)/CN
E23             1       CLDNI PROTEIN (DANIO RERIO CLONE MGC:56243 IMAGE:5601526)/CN
E24             1       CLE 1000A/CN
E25             1       CLE 400/CN

=> E "5-CHLORO-2-DEOXYCYTIDINE"/CN 25
E1              1       5-CHLORO-2-CYCLOPROPYLPYRAZOLO(1,5-A)PYRIMIDINE/CN
E2              1       5-CHLORO-2-CYCLOPROPYLPYRIMIDINE/CN
E3              0 --> 5-CHLORO-2-DEOXYCYTIDINE/CN
E4              1       5-CHLORO-2-DICHLOROACETYLAMINO-O-CHLOROBENZOPHENONE/CN
E5              1       5-CHLORO-2-DICHLOROACETYLAMINO-O-METHYLBENZOPHENONE/CN
E6              1       5-CHLORO-2-DICHLOROACETYLAMINOBENZOPHENONE/CN
E7              1       5-CHLORO-2-DIFLUOROMETHOXYBENZALDEHYDE/CN
E8              1       5-CHLORO-2-DIMETHYLAMINO-3-METHYLBENZOXAZOLIUM IODIDE/CN
E9              1       5-CHLORO-2-DIMETHYLAMINOBENZOIC ACID METHYL ESTER/CN
E10             1       5-CHLORO-2-DODECYLOXYBENZENESULFONYL CHLORIDE/CN
E11             1
5-CHLORO-2-ETHOXY-1-((2-(TRIMETHYLSILANYL)ETHOXY)METHYL)-1H-IMIDAZOLE-4-CARBOXALDEHY
DE/CN
E12             1       5-CHLORO-2-ETHOXY-4-METHOXYBENZENESULFONYL CHLORIDE/CN
E13             1       5-CHLORO-2-ETHOXYANILINE/CN
E14             1       5-CHLORO-2-ETHOXYBENZALDEHYDE/CN
E15             1       5-CHLORO-2-ETHOXYBENZAMIDE/CN
E16             1       5-CHLORO-2-ETHOXYBENZOIC ACID/CN
E17             1       5-CHLORO-2-ETHOXYBENZOTHIAZOLE/CN
E18             1       5-CHLORO-2-ETHOXYBENZOYL CHLORIDE/CN
E19             1       5-CHLORO-2-ETHOXYCARBONYLINDOLE/CN
E20             1       5-CHLORO-2-ETHOXYCARBONYLOXY-4-HYDROXYPYRIDINE/CN
E21             1       5-CHLORO-2-ETHOXYINDOLE/CN
E22             1       5-CHLORO-2-ETHOXYNICOTINIC ACID/CN
E23             1       5-CHLORO-2-ETHOXYPHENOL/CN
E24             1       5-CHLORO-2-ETHOXYPHENYLBORONIC ACID/CN
E25             1       5-CHLORO-2-ETHOXYPYRIDINE/CN

=> E "CHLORO-2-DEOXYCYTIDINE"/CN 25
E1              1       CHLORO-2-(PIPERIDIN-1-YL)ETHANE/CN
E2              1       CHLORO-2-(PYRROLIDIN-1-YL)ETHANE/CN
E3              0 --> CHLORO-2-DEOXYCYTIDINE/CN
E4              1       CHLORO-2-FURYLDIMETHYLSILANE/CN
E5              1       CHLORO-2-FURYLMETHYL ACETATE/CN
E6              1       CHLORO-2-HYDROXYPROPYL METHACRYLATE-DIETHYLENE GLYCOL
DIMETHACRYLATE-METHYL METHACRYLATE COPOLYMER/CN
E7              1       CHLORO-2-NAPHTHYLMERCURY/CN
E8              1       CHLORO-2-NORBORNYLACETIC ANHYDRIDE/CN
E9              1       CHLORO-2-PENTENE/CN
E10             1       CHLORO-2-PHENYLPHENOL/CN
E11             1       CHLORO-2-PROPANONE/CN
E12             1       CHLORO-2-THIENYLCARBENE/CN
E13             1       CHLORO-2-THIENYLZINC/CN
E14             1       CHLORO-3,4-DIMETHOXYBENZOIC ACID METHYL ESTER/CN
E15             1       CHLORO-3-PYRIDYLDIAZIRINE/CN
E16             1       CHLORO-35CL-AMINE/CN
E17             1       CHLORO-35CL-AMINE-15N/CN
E18             1       CHLORO-35CL-AMINE-D/CN
E19             1       CHLORO-35CL-AMINE-D2/CN
E20             1       CHLORO-35CL-CHLORO-37CL-DIFLUOROMETHANE/CN
E21             1       CHLORO-35CL-METHYL METHYL ETHER/CN
E22             1       CHLORO-35CL-METHYL METHYL-13C ETHER/CN
E23             1       CHLORO-35CL-METHYL METHYL-D ETHER/CN
E24             1       CHLORO-35CL-METHYL-13C METHYL ETHER/CN
```

```
E25           1     CHLORO-35CL-METHYL-D METHYL ETHER/CN

=> E "5-CHLORO-2'-DEOXYCYTIDINE"/CN 25
E1            1     5-CHLORO-1H-PYRROLO(3,2-B)PYRIDINE/CN
E2            1     5-CHLORO-2'-CHLORO-4'-NITROSALICYLANILIDE/CN
E3            1 --> 5-CHLORO-2'-DEOXYCYTIDINE/CN
E4            1     5-CHLORO-2'-DEOXYCYTIDINE-5'-TRIPHOSPHATE/CN
E5            1     5-CHLORO-2'-DEOXYURIDINE/CN
E6            1     5-CHLORO-2'-FLUORO-2-(2-HYDROXYETHYL)AMINOBENZOPHENONE/CN
E7            1     5-CHLORO-2'-FLUORO-2-(HYDROXYMETHYL)BENZHYDROL/CN
E8            1     5-CHLORO-2'-FLUORO-2-IODOBENZOPHENONE/CN
E9            1     5-CHLORO-2'-O-METHYLANZIAIC ACID/CN
E10           1     5-CHLORO-2(1H)-PYRIDINETHIONE/CN
E11           1     5-CHLORO-2(1H)-PYRIDONE/CN
E12           1     5-CHLORO-2(1H)-PYRIMIDINONE/CN
E13           1     5-CHLORO-2(1H)-PYRIMIDINONE HYDROCHLORIDE/CN
E14           1     5-CHLORO-2(1H)-PYRIMIDINONE POTASSIUM SALT/CN
E15           1     5-CHLORO-2(3H)-BENZOFURANONE/CN
E16           1     5-CHLORO-2(3H)-BENZOTHIAZOLETHIONE/CN
E17           1     5-CHLORO-2(3H)-BENZOXAZOLETHIONE/CN
E18           1     5-CHLORO-2(3H)-BENZOXAZOLONE/CN
E19           1     5-CHLORO-2(5H)-FURANONE/CN
E20           1     5-CHLORO-2,1,3-BENZOSELENADIAZOLE/CN
E21           1     5-CHLORO-2,1,3-BENZOTHIADIAZOLE/CN
E22           1     5-CHLORO-2,1,3-BENZOXADIAZOLE/CN
E23           1     5-CHLORO-2,1,3-BENZOXADIAZOLE-4-SULFONYL CHLORIDE/CN
E24           1     5-CHLORO-2,1-BENZISOTHIAZOLE/CN
E25           1     5-CHLORO-2,1-BENZISOXAZOLE/CN

=> S E3
L1            1 "5-CHLORO-2'-DEOXYCYTIDINE"/CN

=> DIS L1 1 SQIDE

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   32387-56-7  REGISTRY
CN   Cytidine, 5-chloro-2'-deoxy-  (CA INDEX NAME)
OTHER NAMES:
CN   5-Chloro-2'-deoxycytidine
CN   5-Chlorodeoxycytidine
CN   NSC 371331
FS   STEREOSEARCH
MF   C9 H12 Cl N3 O4
LC   STN Files:   BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT,
       CHEMCATS, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSRESEARCH, MEDLINE,
       PROUSDDR, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)
DT.CA  CAplus document type:  Conference; Dissertation; Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); RACT
       (Reactant or reagent); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
       study); FORM (Formation, nonpreparative); PREP (Preparation); PROC
       (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

41 REFERENCES IN FILE CA (1907 TO DATE)
41 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file medline caplus wpids uspatfull
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.84	9.06

FILE 'MEDLINE' ENTERED AT 13:51:15 ON 31 MAR 2009

FILE 'CAPLUS' ENTERED AT 13:51:15 ON 31 MAR 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'WPIDS' ENTERED AT 13:51:15 ON 31 MAR 2009

FILE 'USPATFULL' ENTERED AT 13:51:15 ON 31 MAR 2009

=> s l1
L2 59 L1

=> s l2 and tetrahydrouridine
L3 26 L2 AND TETRAHYDROURIDINE

=> s l3 and radiation
L4 20 L3 AND RADIATION

=> d l4 1-20 ibib, abs, hitstr

L4 ANSWER 1 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2001644763 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11697326
TITLE: Five-chlorodeoxycytidine, a tumor-selective enzyme-driven radiosensitizer, effectively controls five advanced human tumors in nude mice.
AUTHOR: Greer S; Alvarez M; Mas M; Wozniak C; Arnold D; Knapinska A; Norris C; Burk R; Aller A; Dauphinee M
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Miami School of Medicine, FL 33101, USA.
CONTRACT NUMBER: 1R41CA79272-01A (United States NCI NIH HHS)
SOURCE: International journal of radiation oncology, biology, physics, (2001 Nov 1) Vol. 51, No. 3, pp. 791-806. Journal code: 7603616. ISSN: 0360-3016.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 8 Nov 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 4 Dec 2001

AB PURPOSE: The study's goals were as follows: (1) to extend our past findings with rodent tumors to human tumors in nude mice, (2) to determine if the drug protocol could be simplified so that only CldC and one modulator, tetrahydrouridine (H4U), would be sufficient to obtain efficacy, (3) to determine the levels of deoxycytidine kinase and dCMP deaminase in human tumors, compared to adjacent normal tissue, and (4) to determine the effect of CldC on normal tissue radiation damage to the cervical spinal cord of nude mice. METHODS AND MATERIALS: The five human tumors used were as follows: prostate tumors, PC-3 and H-1579; glioblastoma, SF-295; breast tumor, GI-101; and lung tumor, H-165. The duration of treatment was 3-5 weeks, with drugs administered on Days 1-4 and radiation on Days 3-5 of each week. The biomodulators of CldC were N-(Phosphonacetyl)-L-aspartate (PALA), an inhibitor of aspartyl transcarbamoylase, 5-fluorodeoxycytidine (FdC), resulting in tumor-directed inhibition of thymidylate synthetase, and H4U, an inhibitor of cytidine deaminase. The total dose of focused irradiation of the tumors was usually 45 Gy in 12 fractions. RESULTS: Marked radiosensitization was obtained with CldC and the three modulators. The average days in tumor regrowth delay for X-ray compared to drugs plus X-ray, respectively, were: PC-3 prostate, 42-97; H-1579 prostate, 29-115; glioblastoma, 5-51; breast, 50-80; lung, 32-123. Comparative studies with PC-3 and H-1579 using CldC coadministered with H4U, showed that both PALA and FdC are dispensable, and the protocol can be simplified with equal and possibly heightened efficacy. For example, PC-3 with X-ray and (1) no drugs, (2) CldC plus the three modulators, (3) a high dose of CldC, and (4) escalating doses of CldC resulted in 0/10, 3/9, 5/10, and 6/9 cures, respectively. The tumor regrowth delay data followed a similar pattern. After treating mice only 11/2 weeks with CldC + H4U, 92% of the PC-3 tumor cells were found to possess CldU in their DNA. The great majority of head-and-neck tumors from patient material had markedly higher levels of dC kinase and dCMP deaminase than found in adjacent normal tissue. Physiologic and histologic studies showed that CldC + H4U combined with X-ray, focused on the cervical spinal cord, did not result in damage to that tissue. CONCLUSIONS: 5-CldC coadministered with only H4U is an effective radiosensitizer of human tumors. Ninety-two percent of PC-3 tumor cells have been shown to take up ClUra derived from CldC in their DNA after only 11/2 weeks and 2 weeks of bolus i.p. injections. Enzymatic alterations that make tumors successful have been exploited for a therapeutic advantage. The great electronegativity, coupled with the relatively small Van der Waal radius of the Cl atom, may result in CldC's possessing the dual advantageous properties of FdC on one hand and BrdU and IdU on the other hand. These advantages include autoenhancing the incorporation of CldUTP into DNA by not only overrunning but also inhibiting the formation of competing TTP pools in tumors. A clinical trial is about to begin, with head-and-neck tumors as a first target of CldC radiosensitization.

L4 ANSWER 2 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1995332057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7607927
TITLE: Five-chlorodeoxycytidine and biomodulators of its metabolism result in fifty to eighty percent cures of advanced EMT-6 tumors when used with fractionated

radiation.
AUTHOR: Greer S; Schwade J; Marion H S
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Miami School of Medicine, FL 33101, USA.
SOURCE: International journal of radiation oncology, biology, physics, (1995 Jul 15) Vol. 32, No. 4, pp. 1059-69. Journal code: 7603616. ISSN: 0360-3016.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 28 Aug 1995
Last Updated on STN: 28 Aug 1995
Entered Medline: 17 Aug 1995

AB PURPOSE: To extend our findings in previous radiation and biochemical studies with five rodent tumors, in which we used one and occasionally two or three irradiations. The extent of control of the EMT-6 mammary adenocarcinoma was determined using fractionated radiation (12 irradiations) over a 3-week period using the radiosensitizer 5-chloro-2'-deoxycytidine (CldC) and biomodulators of its metabolism: N-(Phosphonacetyl)-L-aspartate (PALA), tetrahydrouridine and 5-fluoro-2'-deoxycytidine (FdC). METHODS AND MATERIALS: Mammary adenocarcinoma EMT-6 tumors implanted 1 week prior to therapy in BALB/c mice were subjected to single daily doses of focused radiation, not exceeding a total of 60 Gy, on days 2-5 of each week. N-(Phosphonacetyl)-L-aspartate (PALA) was administered on the first day of therapy. Five-fluoro-2'-deoxycytidine and ClcC were administered in the morning and afternoon, respectively, of the next 2 days, and ClcC was administered on the fourth day. Tetrahydrouridine was always coadministered with FdC or ClcC. Drug and radiation treatments overlapped for 3 weeks. RESULTS: Fifty to 80% cures (usually 70%) were obtained with no apparent morbidity and the same moderate weight loss that occurs with radiation alone. Neither tumor regrowth delay nor cures were obtained with drugs or radiation alone. An apparent threefold dose increase effect was obtained with the end point: "days to reach 4 times initial tumor volume." Increasing the radiation dose threefold (without drugs) resulted in four out of five deaths; increasing the dose twofold (without drugs) resulted in extensive weight loss and hair loss in the entire ventral area and no cures. Increasing the dose of drugs or radiation 1.5-fold, in the complete protocol, did not result in increased morbidity. Comparative studies with Iododeoxyuridine demonstrate the heightened efficacy of ClcC. CONCLUSIONS: One cannot achieve the same results obtained with ClcC and the modulators by merely increasing the dose of radiation. There is a significant window of safety in this approach. The evidence we have obtained with EMT-6, the fifth rodent tumor we have studied with ClcC, as well as the demonstrated and proposed reasons for its superior efficacy over 5-Iododeoxyuridine (and 5-Bromodeoxyuridine), drugs in current use, indicate that ClcC will allow more aggressive treatment of human tumors with radiation than is now feasible.

L4 ANSWER 3 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1992138271 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1735688
TITLE: 5-chlorodeoxycytidine, a radiosensitizer effective against RIF-1 and Lewis lung carcinoma, is also effective against a DMBA-induced mammary adenocarcinoma and the EMT-6 tumor in BALB/c mice.
AUTHOR: Greer S; Santos O; Gottlieb C; Schwade J; Marion H S
CORPORATE SOURCE: Department of Microbiology and Immunology, University of

Miami School of Medicine, FL 33136.
SOURCE: International journal of radiation oncology, biology, physics, (1992) Vol. 22, No. 3, pp. 505-10. Journal code: 7603616. ISSN: 0360-3016.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 29 Mar 1992
Last Updated on STN: 29 Mar 1992
Entered Medline: 10 Mar 1992

AB 5-Chlorodeoxycytidine (CldC), coadministered with modulators of pyrimidine metabolism, is an effective radiosensitizer of murine tumors. Past studies that utilized RIF-1 tumors in C3H mice and Lewis lung carcinoma (LLC) in BDF1 mice have been extended with an emphasis on using multiple cycles of drug administration followed by irradiation of LLC and the use of two additional tumor models. Four of seven cures of BDF1 mice bearing LLC were obtained with three doses of 20 Gy irradiation, in which the first and third dose were preceded by a "Standard Protocol" that includes N-(phosphonacetyl)-L-aspartic acid (PALA), 5-fluorodeoxycytidine (FdC), tetrahydrouridine, and the radiosensitizer, 5-chlorodeoxycytidine. No cures were obtained in groups of mice receiving radiation alone or drugs alone, and there were no "no takes" in untreated control groups (six mice/group). Extensive tumor inhibition, exceeding that obtained with drugs or radiation alone, was obtained with two cycles of drugs and radiation combined when a dimethybenzanthracene-induced mammary adenocarcinoma was used in BALB/c mice. With the EMT-6 tumor in BALB/c mice, doses of 10 and 20 Gy were administered 9 and 16 days after tumor implantation, each preceded with the Standard Protocol; this resulted in a tumor growth delay of 24 days. No tumor growth delay occurred with drugs or radiation alone. The omission of PALA, FdC or CldC from the Standard Protocol resulted in loss of tumor control, which was obtained with the complete protocol. The fact that 5-chlorodeoxycytidine is an effective radiosensitizer in four rodent tumor systems is compelling evidence that it has potential as a radiosensitizer of human tumors, especially in view of its tumor selectivity and its resistance to catabolism when used with modulators of its metabolism, and in view of the high levels of the key enzymes in human tumors, which can convert 5-chlorodeoxycytidine to 5-chlorodeoxyuridine triphosphate, the proximate radiosensitizer.

L4 ANSWER 4 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1990368420 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2394614
TITLE: Radiation, pool size and incorporation studies in mice with 5-chloro-2'-deoxycytidine.
AUTHOR: Santos O; Perez L M; Briggle T V; Boothman D A; Greer S B
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Miami, School of Medicine, FL 33101.
CONTRACT NUMBER: CA 33219 (United States NCI NIH HHS)
CA 37791 (United States NCI NIH HHS)
SOURCE: International journal of radiation oncology, biology, physics, (1990 Aug) Vol. 19, No. 2, pp. 357-65. Journal code: 7603616. ISSN: 0360-3016.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 9 Nov 1990
Last Updated on STN: 9 Nov 1990
Entered Medline: 11 Oct 1990

AB Bolus doses of 5-chlorodeoxycytidine (CldC) administered with modulators of pyrimidine metabolism, followed by X-irradiation, resulted in a 2-fold dose increase effect against RIF-1 tumors in C3H mice. Pool size studies of the fate of [14C]-CldC in BDF1 mice bearing Sarcoma-180 tumors, which demonstrated the rapid formation of 5-chlorodeoxycytidylate (CldCMP), and incorporation of CldC as such in RIF-1 tumor DNA, indicate that CldC is a substrate for deoxycytidine kinase, as our past Km studies have shown. Our data indicate that 5-chlorodeoxyuridine triphosphate (CldUTP) accumulates from both the cytidine deaminase-thymidine kinase pathway, as well as from the deoxycytidine kinase-dCMP deaminase pathway, in tumor tissue. As shown in a previous study, tetrahydrouridine (H4U), a potent inhibitor of cytidine deaminase, can effectively inhibit the enzyme in the normal tissues of BDF1 mice. When H4U was administered with the modulators N-(phosphonacetyl)-L-aspartic acid (PALA) and 5-fluorodeoxycytidine (FdC), the levels of CldC-derived RNA and DNA directed metabolites increased in tumor and decreased in normal tissues compared to when CldC was administered alone. These modulators inhibit the de novo pathway of thymidine biosynthesis, lowering thymidine triphosphate (TTP) levels, which compete with CldUTP for incorporation into DNA. 5-Benzylacyclouridine (BAU), an inhibitor of uridine phosphorylase, was also utilized. DNA incorporation studies using C3H mice bearing RIF-1 tumors showed that the extent of incorporation of 5-chlorodeoxyuridine (CldU) into DNA correlates with the levels of cytidine and dCMP deaminases; this is encouraging in view of their high activity in many human malignancies and the low activities in normal tissues, including those undergoing active replication. Up to 3.9% replacement of thymidine by CldU took place in RIF-1 tumors, whereas incorporation into bone marrow was below our limit of detection. CldC did not result in photosensitization under conditions in cell culture in which radiosensitization to X rays was obtained. Thus, the combination of CldC with modulators of its metabolism has potential as a modality of selective radiosensitization for ultimate clinical use in a wider range of tumors than those of the brain.

L4 ANSWER 5 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1989233931 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2715074
TITLE: Selective radiosensitization and cytotoxicity of human melanoma cells using halogenated deoxycytidines and tetrahydrouridine.
AUTHOR: Lawrence T S; Davis M A
CORPORATE SOURCE: Department of Radiation Oncology, University of Michigan, Ann Arbor 48109.
SOURCE: International journal of radiation oncology, biology, physics, (1989 May) Vol. 16, No. 5, pp. 1243-6.
Journal code: 7603616. ISSN: 0360-3016.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
(IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 6 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 19 Jun 1989

AB The halogenated pyrimidines 5-chloro-2'-deoxycytidine (CldCyd) and 5-bromo-2'-deoxycytidine (BrdCyd) can act as radiosensitizers and

cytotoxic agents. It was hypothesized that tumor cells and normal cells might use different metabolic pathways to incorporate these halogenated deoxycytidines into DNA. This difference could potentially be exploited to produce selective radiosensitization and cytotoxicity of human tumor cells compared to normal human fibroblasts. This hypothesis was tested using two human melanoma cell lines and two normal fibroblast cell lines. Either CldCyd or BrdCyd alone caused both cytotoxicity and radiosensitization of tumor and normal cells. The addition of the cytidine deaminase inhibitor tetrahydrouridine (H4U) significantly protected the normal cells but had relatively little effect on the tumor cells. These data indicate that it may be possible to exploit differences between the pyrimidine metabolism of normal cells and melanoma cells to improve the therapeutic index of halogenated pyrimidines both as radiosensitizers and as cytotoxic agents.

L4 ANSWER 6 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1987007839 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3759575
TITLE: Sensitization to X ray by 5-chloro-2'-deoxycytidine co-administered with tetrahydrouridine in several mammalian cell lines and studies of 2'-chloro derivatives.
AUTHOR: Perez L M; Greer S
CONTRACT NUMBER: CA33219 (United States NCI NIH HHS)
SOURCE: International journal of radiation oncology, biology, physics, (1986 Aug) Vol. 12, No. 8, pp. 1523-7. Journal code: 7603616. ISSN: 0360-3016.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO) Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 2 Mar 1990 Last Updated on STN: 3 Feb 1997 Entered Medline: 30 Oct 1986

AB 5-Chloro-2'-deoxycytidine (CldC) + tetrahydrouridine (H4U) sensitizes mammalian cells (HEp-2, RIF-1, S-180) to X ray. This sensitization, as demonstrated previously with HEp-2 cells, is heightened when cells are pre-incubated with inhibitors of pyrimidine synthesis. CHO cells, which intrinsically lack both cytidine deaminase (CD) and deoxycytidylate deaminase (dCMPD), are sensitized to X ray by 5-chlorodeoxyuridine (CldU) but display no significant sensitization with CldC + H4U. The presence and level of these deaminases appears to correlate with X ray sensitization in cell culture. From experiments in cell culture, it can be inferred that one pathway of conversion, deoxycytidine kinase----dCMPD, or CD----thymidine kinase, may be sufficient for metabolizing CldC to a radiosensitizer. However, if both pathways are blocked, as in CHO cells, no X ray sensitization results. In addition to HEp-2 cells, which are extremely elevated in both CD and dCMPD activities, we have examined the sensitization of S-180 and RIF-1 cells to X ray by CldC + H4U. Both cell lines possess an enzymatic profile consistent with their sensitization to X ray by CldC + H4U. Dose enhancement ratios of 1.5 to 1.9 for cells treated with CldC + H4U and ratios of 2.0-2.7 for cells pre-treated with inhibitors of pyrimidine synthesis prior to CldC + H4U have been obtained. Based on reports of the marked X ray sensitization of bacteria by 2'-chloro-2'-deoxythymidine, we obtained 2',5-dichloro-2'-deoxycytidine and 5-bromo-2'-chloro-2-deoxyuridine and found these analogs to be X ray sensitizers of mammalian cells. The strategy that we propose with CldC + H4U and the related 2'-chloro derivatives, based on the elevation of CD and dCMPD in human tumors, offers a degree of selectivity that is not

necessarily related to differences in cell kinetics; such that malignancies other than brain tumors may be amenable to this therapy.

L4 ANSWER 7 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1986189633 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3698014
TITLE: In vitro and in vivo radiation sensitization by the halogenated pyrimidine 5-chloro-2'-deoxycytidine.
AUTHOR: Russell K J; Rice G C; Brown J M
CONTRACT NUMBER: 5 T32 CA 09302-07 (United States NCI NIH HHS)
CA-15201 (United States NCI NIH HHS)
SOURCE: Cancer research, (1986 Jun) Vol. 46, No. 6, pp. 2883-7.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198606
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 25 Jun 1986

AB 5-Chloro-2'-deoxycytidine (Cld/Cyd) is hypothesized to have preferential incorporation into tumor DNA on the basis of elevated deoxycytidine-5'-phosphate deaminase and deoxycytidine kinase levels in tumors. Radiosensitization by Cld/Cyd was evaluated in exponentially growing Chinese hamster ovary cells by determining the ratio of radiation doses in control and treated cells to produce the same degree of cell killing (sensitizer enhancement ratio). Sensitizer enhancement ratios of 1.2-1.8 are seen at Cld/Cyd concentrations of 3-100 microM, 64 h incubation, and 200-600 cGy irradiation. Coincubation with tetrahydrouridine (H4Urd), a proposed inhibitor of Cld/Cyd catabolism by plasma cytidine deaminase resulted in no enhanced drug or radiation cytotoxicity. C3H mice given implants of RIF-1 tumors received 72-h continuous i.p. infusions of Cld/Cyd with or without H4Urd, or 5-bromo-2'-deoxyuridine (BrdUrd). Excised tumors were irradiated as single cell suspensions in vitro. Infusions of equimolar (0.4 mmol/kg/day) Cld/Cyd or BrdUrd resulted in greater radiosensitization by BrdUrd with no potentiation of Cld/Cyd by coinfusion with 0.8 mmol/kg/day H4Urd. Infusions with equitoxic doses of Cld/Cyd (0.8 mmol/kg/day) or BrdUrd (0.4 mmol/kg/day) yielded equal BrdUrd and Cld/Cyd sensitizer enhancement ratios of 1.6, without H4Urd potentiation of Cld/Cyd. Fluorescence-activated cell sorter analysis of tumor cell suspensions using a monoclonal antibody reactive with BrdUrd and Cld/Cyd disclosed a population of noncycling cells in tumors treated with Cld/Cyd/H4Urd that is not seen in tumors exposed to either BrdUrd or Cld/Cyd alone.

L4 ANSWER 8 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1984288944 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6236189
TITLE: Marked radiosensitization of cells in culture to X ray by 5-chlorodeoxycytidine coadministered with tetrahydrouridine, and inhibitors of pyrimidine biosynthesis.
AUTHOR: Perez L M; Mekras J A; Briggle T V; Greer S
SOURCE: International journal of radiation oncology, biology, physics, (1984 Aug) Vol. 10, No. 8, pp. 1453-8.
Journal code: 7603616. ISSN: 0360-3016.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198410
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 24 Oct 1984

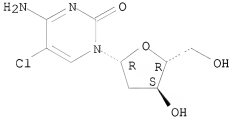
AB Our approach to overcome the problem of rapid catabolism and general toxicity encountered with 5-halogenated analogues of deoxyuridine (5-bromo, chloro or iododeoxyuridine), which has limited their use as tumor radiosensitizers, is to utilize 5-chlorodeoxycytidine (CldC) with tetrahydrouridine (H4U). We propose that CldC, coadministered with H4U, is metabolized in the following manner: CldC----CldCMP----CldUMP----- ----CldUTP----DNA. All the enzymes of this pathway are elevated in many human malignant tumors and in HEp-2 cells. In X irradiation studies with HEp-2 cells, limited to 1 or 2 radiation doses, we have obtained 3.0 to 3.8 apparent dose enhancement ratios (these represent upper limits) when cells are preincubated with inhibitors of pyrimidine biosynthesis: N-(Phosphonacetyl)-L-aspartate (PALA) and 5-fluorodeoxyuridine (FdU) or 5-fluorodeoxycytidine (FdC) + H4U. Optimum conditions for radiosensitization are: PALA (0.1 mg/ml) 18-20 hr prior to FdU (0.1 microM) or FdC (0.02 microM) + H4U (0.1 mM) followed 6 hr later by CldC (0.1-0.2 mM) + H4U (0.1 mM) for 56-68 hr. Viabilities of 10 +/- 4% to 15 +/- 1% (+/- S.E.) were obtained for drug-treated unirradiated cells. Enzymatic studies indicate that this toxicity may be tumor selective. CldC + H4U alone (at these concentrations) results in 20% substitution of CldU for thymidine in DNA (determined by HPLC analysis). Preliminary toxicity studies indicate that mice will tolerate treatment protocols involving a single dose of PALA (200 mg/kg) followed by a dose of FdU (50 mg/kg) and 3 cycles of CldC (500 mg/kg) + H4U (100 mg/kg) at 10 hour intervals, with marginal weight loss (4%). In this approach we seek to obtain preferential conversion of CldC to CldUTP at the tumor site by taking advantage of quantitative differences in enzyme levels between tumors and normal tissues.

L4 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:857776 CAPLUS
DOCUMENT NUMBER: 149:167941
TITLE: Designer therapy of pancreatic tumors
INVENTOR(S): Greer, Sheldon B.
PATENT ASSIGNEE(S): University of Miami, USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008085611	A2	20080717	WO 2007-US85613	20071127
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,			

BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2006-861088P P 20061127
AB Chemotherapeutic and Radiation sensitizing agents which target tumor cells, specifically, based on the elevation of enzyme pathways, provide highly selective drug therapy. These agents are combined with modulating doses of cytidine deaminase inhibitors to increase selectivity. Furthermore, high doses of these cytidine deaminase inhibitors have the potential of counteracting the aggressive and metastatic characteristics of pancreatic tumors. For tumors with high levels of cytidine deaminase, such as pancreatic tumors, this elevation provides a therapeutic approach with prodrugs that require deamination for their activation. For tumors with high levels of uridine/cytidine kinase, a different class of pyrimidine analogs can be activated selectively in tumors for a therapeutic advantage.
IT 32387-56-7, 5-Chlorodeoxycytidine
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(designer therapy of pancreatic tumors using chemotherapeutic and radiosensitizer agents and cytidine deaminase inhibitors in relation to uridine/cytidine kinase)
RN 32387-56-7 CAPLUS
CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:738057 CAPLUS
DOCUMENT NUMBER: 137:17179
TITLE: 5-chlorodeoxycytidine, a tumor-selective enzyme-driven radiosensitizer, effectively controls five advanced human tumors in nude mice
AUTHOR(S): Greer, S.; Alvarez, M.; Mas, M.; Wozniak, C.; Arnold, D.; Knapinska, A.; Norris, C.; Burk, R.; Aller, A.; Dauphinee, M.
CORPORATE SOURCE: Departments of Microbiology and Immunology, Biochemistry and Molecular Biology, Radiation Oncology, Sylvester Cancer Center, University of Miami School of Medicine, Miami, FL, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2001), 51(3), 791-806
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: The study goals were as follows: (1) to extend our past findings with rodent tumors to human tumors in nude mice, (2) to determine if the drug protocol could be simplified so that only CldC and one modulator, tetrahydrouridine (H4U), would be sufficient to obtain efficacy, (3) to determine the levels of deoxycytidine kinase and dCMP deaminase in human tumors, compared to adjacent normal tissue, and (4) to determine the effect of CldC on normal tissue radiation damage to the cervical spinal

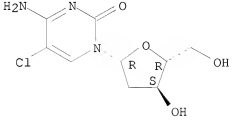
cord of nude mice. Methods and Materials: The five human tumors used were as follows: prostate tumors, PC-3 and H-1579; glioblastoma, SF-295; breast tumor, GI-101; and lung tumor, H-165. The duration of treatment was 3-5 wk, with drugs administered on Days 1-4 and radiation on Days 3-5 of each week. The biomodulators of CldC were N-(Phosphonacetyl)-L-aspartate (PALA), an inhibitor of aspartyl transcarbamoylase, 5-fluorodeoxycytidine (FdC), resulting in tumor-directed inhibition of thymidylate synthetase, and H4U, an inhibitor of cytidine deaminase. The total dose of focused irradiation of the tumors was usually 45 Gy in 12 fractions. Results: Marked radiosensitization was obtained with CldC and the three modulators. The average days in tumor regrowth delay for X-ray compared to drugs plus X-ray, resp., were: PC-3 prostate, 42-97; H-1579 prostate, 29-115; glioblastoma, 5-51; breast, 50-80; lung, 32-123. Comparative studies with PC-3 and H-1579 using CldC coadministered with H4U, showed that both PALA and FdC are dispensable, and the protocol can be simplified with equal and possibly heightened efficacy. For example, PC-3 with X-ray and (1) no drugs, (2) CldC plus the three modulators, (3) a high dose of CldC, and (4) escalating doses of CldC resulted in 0/10, 3/9, 5/10, and 6/9 cures, resp. The tumor regrowth delay data followed a similar pattern. After treating mice only 1 wk with CldC +H4U, 92% of the PC-3 tumor cells were found to possess CldU in their DNA. The great majority of head-and-neck tumors from patient material had markedly higher levels of dC kinase and dCMP deaminase than found in adjacent normal tissue. Physiol. and histol. studies showed that CldC +H4U combined with X-ray, focused on the cervical spinal cord, did not result in damage to that tissue. Conclusions: 5-CldC coadministered with only H4U is an effective radiosensitizer of human tumors. Ninety-two percent of PC-3 tumor cells have been shown to take up ClUra derived from CldC in their DNA after only 1 wk and 2 wk of bolus i.p. injections. Enzymic alterations that make tumors successful have been exploited for a therapeutic advantage. The great electronegativity, coupled with the relatively small Van der Waal radius of the Cl atom, may result in CldC possessing the dual advantageous properties of FdC on one hand and BrdU and IdU on the other hand. These advantages include autoenhancing the incorporation of CldUTP into DNA by not only overrunning but also inhibiting the formation of competing TTP pools in tumors. A clin. trial is about to begin, with head-and-neck tumors as a first target of CldC radiosensitization.

IT 32387-56-7, 5-Chlorodeoxycytidine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor action mechanism of chlorodeoxycytidine alone or in combination with other radiosensitizers)

RN 32387-56-7 CAPLUS

CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:628023 CAPLUS
DOCUMENT NUMBER: 133:219596
TITLE: Dramatic simplification of a method to treat neoplastic disease by radiation
INVENTOR(S): Greer, Sheldon B.
PATENT ASSIGNEE(S): Halogenetics, Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051639	A2	20000908	WO 2000-US2530	20000301
WO 2000051639	A3	20010111		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6933287	B1	20050823	US 2000-514278	20000228
EP 1156827	A2	20011128	EP 2000-911684	20000301
EP 1156827	B1	20060920		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
AT 339960	T	20061015	AT 2000-911684	20000301
ES 2273672	T3	20070516	ES 2000-911684	20000301
US 20040192639	A1	20040930	US 2004-779746	20040218

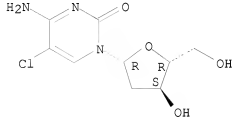
PRIORITY APPLN. INFO.:
US 1999-122479P P 19990301
US 2000-514278 A3 20000228
WO 2000-US2530 W 20000301

AB The present invention is related to agents useful in the treatment of tumors by radiation by sensitizing tumor cells toward the radiation. The agents of the invention can perform selective tumor radiosensitization and be involved in tumor directed hypomethylation. The agents of the invention include (a) 5-chloro-2'-deoxycytidine (CldC) administered without a cytidine deaminase inhibitor, (b) CldC administered with a cytidine deaminase inhibitor, (c) CldC and 4-N-methylamino 5-fluoro-2'-deoxycytidine (4-N-methylamino FdC), or (d) CldC and 4-N-methylamino FdC coadministered with a cytidine deaminase inhibitor. The cytidine deaminase inhibitor can be tetrahydrouridine or Zebularine. Within the scope of the invention are methods of treating tumors by administering the agents of the present invention without the need of other modulators of metabolism Another aspect of the invention is a method of hypomethylating a gene silenced in a tumor of a subject by administering the agents of the invention to the subject to reduce the aggressiveness of the tumor, the metastatic propensity of the tumor, the genetic instability of the tumor, and/or the resistance of the tumor to drug or radiation treatment. An addnl. aspect of the invention is a method of protecting normal tissues during a radiation treatment of a tumor in a subject by administering the agents of the invention to the subject before or during the radiation treatment. The agents of the invention can be combined with new sources or new schedules of radiation, and new categories of tumors can also be treated with the agents of the invention.

IT 32387-56-7, 5-Chloro-2'-deoxycytidine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating neoplastic disease by radiosensitization and tumor directed hypomethylation)
RN 32387-56-7 CAPLUS
CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:732651 CAPLUS
DOCUMENT NUMBER: 123:187874
ORIGINAL REFERENCE NO.: 123:33089a,33092a
TITLE: Five-chlorodeoxycytidine and biomodulators of its metabolism result in fifty to eighty percent cures of advanced EMT-6 tumors when used with fractionated radiation
AUTHOR(S): Greer, Sheldon; Schwade, James; Marion, H. Stan
CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. Miami Sch. Med., Miami, FL, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (1995), 32(4), 1059-69
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Pergamon
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: to extend our findings in previous radiation and biochem. studies with five rodent tumors, in which we used one and occasionally two or three irradns. The extent of control of the EMT-6 mammary adenocarcinoma was determined using fractionated radiation (12 irradns.) over a 3-wk period using the radiosensitizer 5-chloro-2'-deoxycytidine (CldC) and biomodulators of its metabolism: N-(phosphonacetyl)-L-aspartate (PALA), tetrahydrouridine and 5-fluoro-2'-deoxycytidine (FdC). Methods and Materials: mammary adenocarcinoma EMT-6 tumors implanted 1 wk prior to therapy in BALB/c mice were subjected to single daily doses of focused radiation, not exceeding a total of 60 Gy, on days 2-5 of each wk. PALA was administered on the first day of therapy. 5-Fluoro-2'-deoxycytidine and CldC were administered in the morning and afternoon, resp., of the next 2 days, and CldC was administered on the fourth day. Tetrahydrouridine was always coadministered with FdC or CldC. Drug and radiation treatments overlapped for 3 wks. Results: fifty to 80% cures (usually 70%) were obtained with no apparent morbidity and the same moderate weight loss that occurs with radiation alone. Neither tumor regrowth delay nor cures were obtained with drugs or radiation alone. An apparent threefold dose increase effect was obtained with the end point: "days to reach 4 times initial tumor volume". Increasing the radiation dose threefold (without drugs) resulted in four out of

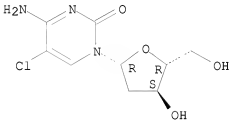
five deaths; increasing the dose twofold (without drugs) resulted in extensive weight loss and hair loss in the entire ventral area and no cures. Increasing the dose of drugs or radiation 1.5-fold, in the complete protocol, did not result in increased morbidity. Comparative studies with Iododeoxyuridine demonstrate the heightened efficacy of CldC. Conclusions: one cannot achieve the same results obtained with CldC and the modulators by merely increasing the dose of radiation. There is a significant window of safety in this approach. The evidence we have obtained with EMT-6, the fifth rodent tumor we have studied with CldC, as well as the demonstrated and proposed reasons for its superior efficacy over 5-Iododeoxyuridine (and 5-Bromodeoxyuridine), drugs in current use, indicate that CldC will allow more aggressive treatment of human tumors with radiation than is now feasible.

IT 32387-56-7, 5-Chloro-2'-deoxycytidine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of mammary adenocarcinoma with chlorodeoxycytidine and radiotherapy)

RN 32387-56-7 CAPLUS

CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1992:190295 CAPLUS

DOCUMENT NUMBER: 116:190295

ORIGINAL REFERENCE NO.: 116:32131a,32134a

TITLE: 5-Chlorodeoxycytidine, a radiosensitizer effective against RIF-1 and Lewis lung carcinoma, is also effective against a DMBA-induced mammary adenocarcinoma and the EMT-6 tumor in BALB/c mice

AUTHOR(S): Greer, Sheldon; Santos, Orlando; Gottlieb, Charles; Schwade, James; Marion, H. Stan

CORPORATE SOURCE: Sch. Med., Univ. Miami, Miami, FL, 33136, USA

SOURCE: International Journal of Radiation Oncology, Biology, Physics (1992), 22(3), 505-10
CODEN: IOBPD3; ISSN: 0360-3016

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 5-Chlorodeoxycytidine (CldC), coadministered with modulators of pyrimidine metabolism, is an effective radiosensitizer of murine tumors. Past studies that utilized RIF-1 tumors in C3H mice and Lewis lung carcinoma (LLC) in BDF1 mice have been extended with an emphasis on using multiple cycles of drug administration followed by irradiation of LLC and the use of two addnl. tumor models. Four of 7 cures of BDF1 mice bearing LLC were obtained with 3 doses of 20 Gy irradiation, in which the first and third dose were preceded by a "Standard Protocol" that includes N-(phosphonacetyl)-L-aspartic acid (PALA), 5-fluorodeoxycytidine (FdC), tetrahydrouridine, and the radiosensitizer, 5-chlorodeoxycytidine. No cures were obtained in groups of mice receiving radiation alone or drugs alone, and there were

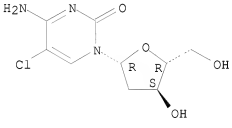
no "no takes" in untreated control groups (6 mice/group). Extensive tumor inhibition, exceeding that obtained with drugs or radiation alone, was obtained with 2 cycles of drugs and radiation combined when a dimethylbenzanthracene-induced mammary adenocarcinoma was used in BALB/c mice. With the EMT-6 tumor in BALB/c mice, doses of 10 and 20 Gy were administered 9 and 16 days after tumor implantation, each preceded with the Standard Protocol; this resulted in a tumor growth delay of 24 days. No tumor growth delay occurred with drugs or radiation alone. The omission of PALA, FdC or CldC from the Standard Protocol resulted in loss of tumor control, which was obtained with the complete protocol. The fact that 5-chlorodeoxycytidine is an effective radiosensitizer in 4 rodent tumor systems is compelling evidence that it has potential as a radiosensitizer of human tumors, especially in view of its tumor selectivity and its resistance to catabolism when used with modulators of its metabolism, and in view of the high levels of the key enzymes in human tumors, which can convert 5-chlorodeoxycytidine to 5-chlorodeoxyuridine triphosphate, the proximate radiosensitizer.

IT 32387-56-7, 5-Chlorodeoxycytidine
RL: BIOL (Biological study)
(radiosensitizer, for lung carcinoma and mammary adenocarcinoma)

RN 32387-56-7 CAPLUS

CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1988:2749 CAPLUS

DOCUMENT NUMBER: 108:2749

ORIGINAL REFERENCE NO.: 108:547a,550a

TITLE: Potentiation of halogenated pyrimidine radiosensitizers in human carcinoma cells by β-lapachone (3,4-dihydro-2,2-dimethyl-2H-naphtho[1,2-b]pyran-5,6-dione), a novel DNA repair inhibitor

AUTHOR(S): Boothman, David A.; Greer, Sheldon; Pardee, Arthur B.

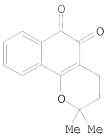
CORPORATE SOURCE: Dana Farber Cancer Inst., Harvard Med. Sch., Boston, MA, 02115, USA

SOURCE: Cancer Research (1987), 47(20), 5361-6
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



Me Me I

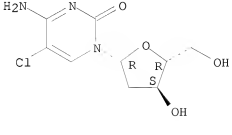
AB β-Lapachone (I) is a novel DNA repair inhibitor. It was tested for synergistic x-ray-induced lethality in combination with several halogenated pyrimidine radiosensitizers. Logarithmic-phase growing human epidermoid laryngeal carcinoma (HEp-2) cells were allowed to incorporate pyrimidine analogs for 48 h (.apprx.2 cell doublings) and then were x-irradiated and subjected to various posttreatments. I synergistically increased the dose enhancement ratios (DERs) of all analogs screened, with the exception of the 2'-chloro derivative of 5-bromodeoxyuridine. For example, following 5-bromodeoxycytidine sensitization, an x-ray DER value of 1.87 at 1% survival was increased to 3.51 due to a 4-h post-x-irradiation exposure to 4 μM I. Do (Mean LD) and Dq (quasi-threshold dose) values for halogenated pyrimidine-sensitized human epidermoid laryngeal carcinoma cells were decreased 1.4-5.4-fold and 1.4-4.0-fold, resp. I had little effect upon the cytotoxicities of unirradiated human epidermoid laryngeal carcinoma cells whether or not they were previously exposed to any of the halogenated pyrimidine radiosensitizers. I treatment following x-irradiation of cell that had not incorporated a pyrimidine analog exhibited DER values of 1.38 and 1.40 at 10 and 1% survival levels, resp. I enhanced the radiosensitization of deoxycytidine analog to a greater extent than the structurally related deoxyuridine analogs. Greater DERs and lower Do and Dq values were found for deoxycytidine than for deoxyuridine analog radiosensitizers following I treatment. This agent may improve presently used radiation therapies and enhance proposed strategies which utilize deoxycytidine analog radiosensitization together with protection of normal tissues by tetrahydrouridine to achieve tumor-selective radiotherapy.

IT 32387-56-7, 5-Chloro-2'-deoxycytidine
RL: BIOL (Biological study)
(radiosensitization by, of human carcinoma cells x-rays, lapachone potentiation of)

RN 32387-56-7 CAPLUS

CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1986:438294 CAPLUS

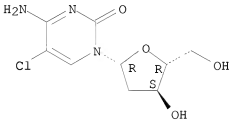
DOCUMENT NUMBER: 105:38294

ORIGINAL REFERENCE NO.: 105:6285a,6288a
TITLE: In vitro and in vivo radiation sensitization by the halogenated pyrimidine 5-chloro-2'-deoxycytidine
AUTHOR(S): Russell, Kenneth J.; Rice, Glenn C.; Brown, J. Martin
CORPORATE SOURCE: Med. Cent., Stanford Univ., Stanford, CA, 94305, USA
SOURCE: Cancer Research (1986), 46(6), 2883-7
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 5-Chloro-2'-deoxycytidine (Cld/Cyd) is hypothesized to have preferential incorporation into tumor DNA on the basis of elevated deoxycytidine-5'-phosphate deaminase and deoxycytidine kinase levels in tumors. Radiosensitization by Cld/Cyd was evaluated in exponentially growing Chinese hamster ovary cells by determining the ratio of radiation doses in control and treated cells to produce the same degree of cell killing (sensitizer enhancement ratio). Sensitizer enhancement ratios of 1.2-1.8 are seen at Cld/Cyd concns. of 3-100 μM, 64 h incubation, and 200-600 cGy x-irradiation Coincubation with tetrahydrouridine (H4Urd), a proposed inhibitor of Cld/Cyd catabolism by plasma cytidine deaminase, resulted in no enhanced drug or radiation cytotoxicity. C3H mice given implants of RIF-1 tumors received 72-h continuous i.p. infusions of Cld/Cyd with or without H4Urd, or 5-bromo-2'-deoxyuridine (BrdUrd). Excised tumors were irradiated as single cell suspensions in vitro. Infusions of equimolar (0.4 mmol/kg/day) Cld/Cyd or BrdUrd resulted in greater radiosensitization by BrdUrd with no potentiation of Cld/Cyd by coinfusion with 0.8 mmol/kg/day H4Urd. Infusions with equitoxic doses of Cld/Cyd (0.8 mmol/kg/day) or BrdUrd (0.4 mmol/kg/day) yielded equal BrdUrd and Cld/Cyd sensitizer enhancement ratios of 1.6, without H4Urd potentiation of Cld/Cyd. Fluorescence-activated cell sorter anal. of tumor cell suspensions using a monoclonal antibody reactive with BrdUrd and Cld/Cyd disclosed a population of noncycling cells in tumors treated with Cld/Cyd/H4Urd that is not seen in tumors exposed to either BrdUrd or Cld/Cyd alone.

IT 32387-56-7
RL: BIOL (Biological study)
(radiosensitization by, of CHO cells and neoplasms)
RN 32387-56-7 CAPLUS
CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



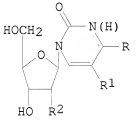
L4 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1985:476273 CAPLUS
DOCUMENT NUMBER: 103:76273
ORIGINAL REFERENCE NO.: 103:12215a,12218a
TITLE: Method and materials for sensitizing neoplastic tissue to radiation
INVENTOR(S): Greer, Sheldon B.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8501871	A1	19850509	WO 1984-US1735	19841026
W: AU, BR, DK, FI, JP, US				
RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
AU 8436107	A	19850522	AU 1984-36107	19841026
AU 583801	B2	19890511		
EP 160079	A1	19851106	EP 1984-904049	19841026
EP 160079	B1	19900131		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
JP 61500224	T	19860206	JP 1984-504070	19841026
JP 05086376	B	19931210		
AT 49894	T	19900215	AT 1984-904049	19841026
US 4894364	A	19900116	US 1985-749540	19850624
CA 1269658	A1	19900529	CA 1985-494396	19851101

PRIORITY APPLN. INFO.:
US 1983-545693 A2 19831026
EP 1984-904049 A 19841026
WO 1984-US1735 A 19841026

GI



I

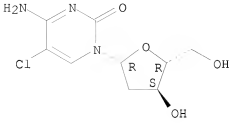
AB I (R = NH2 or O, R1 and R2 = H or halogen) for use in pharmaceutical compns. are radiosensitizers. The concentration of the active ingredient in the composition is 0.01-25% by weight depending on the route of administration, severity of the case, frequency of administration, etc. The radiation dose, x- or γ-ray will be either the same or one-fourth to three-fourths the dose given to patients not receiving the pretreatment sensitizer, and this will result in either a more effective tumor kill or an equal tumor kill but with less damage to underlying tissues. In a toxicity study in animals injected i.p. with N-(phosphonoacetyl)-L-aspartate [51321-79-0] (pretreatment agent) 200, followed 24 h later with i.p. 5-fluoro-2'-deoxyuridine (I; R = NH2, R1 = F, R2 = H) [50-91-9] 50, and 4 h later i.p. 5-chloro-2'-deoxycytidine (I; R = NH2, R1 = Cl, R2 = H) [32387-56-7] 500 coadministered with tetrahydrouridine [18771-50-1] 100 mg, the last 2 compds. administered at the same concentration twice at 10 h intervals, a 4% weight loss occurred which is trivial compared to normal weight loss which occurs from administration of antitumor agents in radiation therapy.

IT 32387-56-7
RL: BIOL (Biological study)
(radiosensitizer composition containing)

RN 32387-56-7 CAPLUS

CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



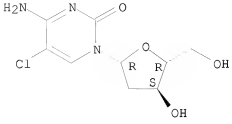
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1984:625942 CAPLUS
DOCUMENT NUMBER: 101:225942
ORIGINAL REFERENCE NO.: 101:34219a,34222a
TITLE: Marked radiosensitization of cells in culture to x-ray by 5-chlorodeoxycytidine coadministered with tetrahydrouridine, and inhibitors of pyrimidine biosynthesis
AUTHOR(S): Perez, Liliana M.; Mekras, John A.; Briggle, Thomas V.; Greer, Sheldon
CORPORATE SOURCE: Sch. Med., Univ. Miami, Miami, FL, 33101, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (1984), 10(8), 1453-8
CODEN: IOBPD3; ISSN: 0360-3016
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To overcome the problem of rapid catabolism and general toxicity encountered with 5-halogenated analogs of deoxyuridine (5-bromo, chloro, or iododeoxyuridine), which has limited their use as tumor radiosensitizers, 5-chlorodeoxycytidine (CldC) with tetrahydrouridine (H4U) is utilized. In x-irradiation studies with HEp-2 cells, limited to 1 or 2 radiation doses, 3.0-3.8 apparent dose enhancement ratios (these represent upper limits) were obtained when cells are preincubated with inhibitors of pyrimidine biosynthesis, i.e., N-(phosphonacetyl)-L-aspartate (PALA) and 5-fluorodeoxyuridine (FdU) or 5-fluorodeoxycytidine (FdC) + H4U. Optimum conditions for radiosensitization are PALA (0.1 mg/mL) 18-20 h prior to FdU (0.1 μM) or FdC (0.02 μM) + H4U (0.1 mM) followed 6 h later by CldC (0.1-0.2 mM) + H4U (0.1 mM) for 56-68 h. Viabilities of 10-15% were obtained for drug-treated unirradiated cells. Enzymic studies indicate that this toxicity may be tumor selective. CldC + H4U alone (at these concns.) results in 20% substitution of CldU for thymidine in DNA (determined by HPLC anal.). Preliminary toxicity studies indicate that mice will tolerate treatment protocols involving a single dose of PALA (200 mg/kg) followed by a dose of FdU (50 mg/kg) and 3 cycles of CldC (500 mg/kg) + H4U (100 mg/kg) at 10 h intervals, with marginal weight loss (4%). In this approach, preferential conversion of CldC to CldUTP at the tumor site is obtained by taking advantage of quant. differences in enzyme levels between tumors and normal tissues.

IT 32387-56-7
RL: BIOL (Biological study)
(radiosensitization by tetrahydrouridine coadministration with, of cells in culture)
RN 32387-56-7 CAPLUS
CN Cytidine, 5-chloro-2'-deoxy- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 18 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2005:211182 USPATFULL
TITLE: Dramatic simplification of a method to treat neoplastic disease by radiation
INVENTOR(S): Greer, Sheldon B., 3600 Mystic Pointe Dr., LPH9, Aventura, FL, UNITED STATES 33180

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6933287	B1	20050823
APPLICATION INFO.:	US 2000-514278		20000228 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-122479P	19990301 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Cook, Rebecca
LEGAL REPRESENTATIVE: Rothwell, Figg, Ernst & Manbeck, P.C.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1518
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of treating tumors with radiation is disclosed, wherein the tumor is sensitized by administering a tumor sensitizing agent comprising 5-chloro-2'-deoxycytidine, 4-N-methyl FdC and a cytidine deaminase inhibitor to a patient having the tumor. The tumor is then subjected to radiation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 19 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2004:248039 USPATFULL
TITLE: Dramatic simplification of a method to treat neoplastic disease by radiation
INVENTOR(S): Greer, Sheldon B., Miami, FL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20040192639	A1	20040930
APPLICATION INFO.:	US 2004-779746	A1	20040218 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-514278, filed on 28 Feb 2000, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-122479P	19990301 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROTHWELL, FIGG, ERNST & MANBECK, P.C., 1425 K STREET, N.W., SUITE 800, WASHINGTON, DC, 20005
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1438
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of treating tumors with radiation is disclosed, wherein the tumor is sensitized by administering a tumor sensitizing agent comprising 5-chloro-2'-deoxycytidine, 4-N-methyl FdC and a cytidine deaminase inhibitor to a patient having the tumor. The tumor is then subjected to radiation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 20 OF 20 USPATFULL on STN
ACCESSION NUMBER: 90:4372 USPATFULL
TITLE: Method and materials for sensitizing neoplastic tissue to radiation
INVENTOR(S): Greer, Sheldon B., 8320 SW 86 Ter., Miami, FL, United States 33143

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4894364		19900116	
	WO 8501871		19850509	
APPLICATION INFO.:	US 1985-749540		19850624	(6)
	WO 1984-US1735		19841026	
			19841026	PCT 371 date
			19010101	PCT 102(e) date

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1983-545693, filed on 26 Oct 1983, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lilling, Herbert J.
LEGAL REPRESENTATIVE: Armstrong, Nikaido, Marmelstein, Kubovcik & Murray
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 640
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Tumors are sensitized to radiation by administration of 5-chlorodeoxycytidine (5-CldC) or 5-halo-2'-halo-2'-deoxy-cytidine or -uridine derivatives. Tetrahydrouridane (H.sub.4 U) and/or 2'-deoxytetrahydrouridine (dH.sub.4 U) is preferably coadministered with the deoxycytidine derivative to inhibit deamination of the deoxycytidine derivatives. Optional pre- or concurrent treatment with agents to reduce the amount of competing metabolites to favor CldC, such as 5-fluorodeoxyuridine, results in a procedure that significantly increases the dose effects of X-radiation. Pharmaceutical compositions suitable for the sensitization of tumors to radiation are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 13:49:17 ON 31 MAR 2009)

FILE 'REGISTRY' ENTERED AT 13:49:29 ON 31 MAR 2009

```
                E "5-CLDC"/CN 25
                E "CLDC"/CN 25
                E "5-CHLORO-2-DEOXYCYTIDINE"/CN 25
                E "CHLORO-2-DEOXYCYTIDINE"/CN 25
                E "5-CHLORO-2'-DEOXYCYTIDINE"/CN 25
L1            1 S E3

     FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 13:51:15 ON 31 MAR
     2009
L2           59 S L1
L3           26 S L2 AND TETRAHYDROURIDINE
L4           20 S L3 AND RADIATION

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    74.53      83.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -7.38      -7.38

STN INTERNATIONAL LOGOFF AT 13:54:38 ON 31 MAR 2009
```